

CLAIMS

We claim:

1. A method for downregulating estrogen receptors in a population of cells expressing an estrogen receptor comprising delivering to said population of cells an effective amount of at least one adenosine analog and a pharmaceutically acceptable carrier to down-regulate estrogen receptor levels.
2. The method of claim 1, wherein the population of cells comprise malignant cells.
3. The method of claim 2, wherein the malignant cells are breast cancer cells.
4. The method of claim 2 or 3, wherein the population of cells are estrogen receptor alpha positive.
5. The method of claim 1, wherein the adenosine analog is an adenosine A3 receptor agonist.
6. The method of claim 5, wherein the adenosine analog is N⁶-(3-iodobenzyl)adenosine-5'-N-methyluronamide or a derivative thereof.
7. The method of claim 5, wherein the adenosine analog is 2-chloro-adenosine or a derivative thereof.
8. The method of claim 1, wherein the downregulation of estrogen receptor levels results from decrease in estrogen receptor transcription.
9. The method of claim 1, wherein at least one cell in the population of cells is or has become resistant to (Z)1,2-diphenyl-1-[4-[2-(dimethylamino)ethoxy]phenyl]-1-butene, 4-OH-(Z)1,2-diphenyl-1-[4-[2-(dimethylamino)ethoxy]phenyl]-1-butene, raloxifene, or N-(n-butyl)-11-[3,17 β -dihydroxyestra-1,3,5(10)-trien-7 α -yl]N- methylundecanamide or a derivative thereof.
10. The method of claim 1, wherein the at least one adenosine analog and a pharmaceutically acceptable carrier to decrease estrogen receptor levels are delivered

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before, after or simultaneously with (Z)1,2-diphenyl-1-[4-[2-(dimethylamino)ethoxy]phenyl]-1-butene, 4-OH-(Z)1,2-diphenyl-1-[4-[2-(dimethylamino)ethoxy]phenyl]-1-butene, raloxifene, or N-(n-butyl)-11-[3,17 β -dihydroxyestra-1,3,5(10)-trien-7 α -yl]N- methylundecanamide or other estrogen receptor regulating pharmaceutical, or a combination thereof.

11. The method of claim 1, wherein at least one cell in the population of cells is growing via anchorage-independent manner.

12. The method of claim 1, wherein at least one cell in the population of cells is growing via anchorage-dependent manner.

13. The method of claim 4, wherein the population of cells comprise at least one cell which is estrogen receptor alpha positive.

14. A method of suppressing cell cycle and/or cellular growth in a population of cells comprising delivering to the cell population an effective amount to downregulate estrogen receptor levels, at least one adenosine analog and a pharmaceutically acceptable carrier.

15. The method of claim 14, wherein the population of cells comprises malignant cells.

16. The method of claim 15, wherein the malignant cells are breast cancer cells.

17. The method of claim 15, wherein the malignant cells are ovarian cancer cells.

18. A method of treating an individual affected with malignant cell growth in a tissue or plurality of tissues expressing estrogen receptors, the method comprising administering to the individual a sufficient amount of an adenosine agonist to downregulate estrogen receptors in a cell population in the tissue or plurality of tissues and a pharmaceutically acceptable carrier.

19. The method of claim 18, wherein the malignant cell growth is breast cancer.

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20. The method of claim 18, wherein the malignant cell growth is ovarian cancer.
21. The method of claim 18, wherein the malignant cell growth is anchorage-independent.
22. The method of claim 18, wherein at least one of the estrogen receptors expressed by the cell population is mutated or truncated.
23. The method of claim 18, wherein the estrogen receptor is estrogen receptor alpha.
24. The method of claim 23, wherein the malignant cell growth is breast cancer or ovarian cancer.
25. A method of identifying a compound suitable for treating malignant cell growth in a tissue which expresses estrogen receptors, the method comprising measuring the amount of estrogen receptor expression in a cell, administering an adenosine analog to the cell, and measuring the expression of estrogen receptor after administration of the adenosine analogue, wherein reduction in the amount of estrogen receptor in the cell after administration of the adenosine analogue indicates identification of a compound suitable for treating malignant cell growth.
26. The method of claim 25, wherein the malignant cell growth is breast cancer or ovarian cancer.
27. Use of at least one adenosine analog in a pharmaceutically acceptable carrier to downregulate estrogen receptors in a population of cells expressing estrogen receptors.
28. The use of the adenosine analog according to claim 27, wherein the cell population is breast or ovarian cancer.
29. The use of the adenosine analog according to claim 27, wherein the cell population exhibits anchorage-independent growth.
30. The use of an adenosine analog according to claim 27, wherein the adenosine analog is adenosine A3 receptor agonist.

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31. The use of an adenosine analog according to claim 27, wherein the adenosine analog is N⁶-(3-iodobenzyl)adenosine-5'-N-methyluronamide or a derivative thereof.

32. The use of an adenosine analog according to claim 27, wherein the adenosine analog is 2-chloro-adenosine or a derivative thereof.

33. A kit for downregulating estrogen receptors in a population of cells comprising in a container at least one adenosine analog capable of downregulating estrogen receptors in the population of cells in a pharmaceutically acceptable carrier in a vial or tube, a means for detecting downregulation of estrogen receptors in the population of cells, and an instruction manual exemplifying how to measure estrogen receptor downregulation using the means provided in the kit.

34. The kit according to claim 33, wherein the adenosine analog is an adenosine A3 receptor agonist.

35. The kit according to claim 33, wherein the adenosine analog is N⁶-(3-iodobenzyl)adenosine-5'-N-methyluronamide or a derivative thereof.

36. The kit according to claim 33, wherein the adenosine analog is, wherein the adenosine analog is 2-chloro-adenosine or a derivative thereof.

37. A kit for detecting compounds capable of downregulating estrogen receptors in a population of cells comprising:

a population of test cells expressing estrogen receptors in a suitable cell growth medium or freezing medium or storage medium;

a standard adenosine analog capable of downregulating estrogen receptors in the population of test cells as powder or in a suitable buffer with known concentration;

a means for detecting estrogen downregulation in the test cell population; and

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an instruction manual outlining exemplary cell growth conditions to detect downregulation of estrogen receptors in the test cell population using the standard adenosine analog.

38. The kit according to claim 37, wherein the test cell population comprises malignant cells.

39. The kit according to claim 37, wherein the malignant cells are breast and/or ovarian cancer cells.

40. The kit according to claim 37, wherein the malignant cells are resistant to (Z)1,2-diphenyl-1-[4-[2-(dimethylamino) ethoxy]phenyl]-1-butene, 4-OH-(Z)1,2-diphenyl-1-[4-[2-(dimethylamino) ethoxy]phenyl]-1-butene, raloxifene, or N-(n-butyl)-11-[3,17 β -dihydroxyestra-1,3,5(10)-trien-7 α -yl]N- methylundecanamide.

41. The kit according to claim 37, wherein the standard adenosine analog is an adenosine A3 receptor agonist.

42. The kit according to claim 37, wherein the standard adenosine analog is N⁶-(3-iodobenzyl)adenosine-5'-N-methyluronamide.

43. The kit according to claim 37, wherein the standard adenosine analog is 2-chloro-adenosine.

44. A pharmaceutical composition for suppressing cell cycle and/or cellular growth comprising an effective amount of at least one adenosine analog and a pharmaceutically acceptable carrier.

45. The pharmaceutical composition according to claim 44, wherein the adenosine analog is an adenosine A3 receptor agonist.

46. The pharmaceutical composition according to claim 44, wherein the adenosine analog is N⁶-(3-iodobenzyl)adenosine-5'-N-methyluronamide or a derivative thereof.

47. The pharmaceutical composition according to claim 44, wherein the adenosine analog is 2-chloro-adenosine or a derivative thereof.